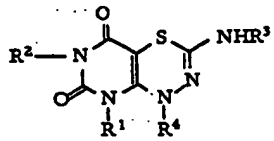
R0144B

B2/B3

31033A/17 B02 TAKE 25.08.76
TAKEDA CHEMICAL IND KK *J5 3028-192

25.08.76-JA-101923 *(16.03.78)* A61k-31/50 C07d-239/54 C07d-Pyrimido (4,5-e) (1,3,4)thiodiazine derivs. - with hypotensive, diuretic, antiinflammatory, gastric secretion inhibiting and cyclic-AMP phosphodiesterase inhibiting activity

(A) Pyrimido[4,5-e][1,3,4]thiadiazine derivs. of formula (I) and salts thereof are new:



(I)

(R^1, R^2 = H or alkyl;
R^3 = H, alkyl, alkenyl, opt. substd. aryl, aralkyl or acyl;
R^4 = H, alkyl or acyl;
provided R^1, R^2 = alkyl when R^4 = acyl).

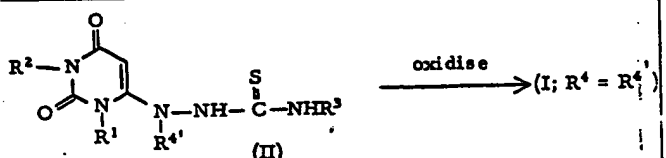
(B) Uracil deriv. intermediates of formula (II) (see "Preparation") are new.

USE

(I) and salts exhibit c-AMP phosphodiesterase inhibition, histamine H_2-receptor inhibition and, esp. to mammals (such as human, dog, rabbit, rat and mouse), hypotensive, diuretic, antiinflammatory and gastric secretion inhibitory activities and are useful as anti-hypertensive, diuretic, antiinflammatory and antiulcer remedies as well as antibacterials and biochemical reagents.

B(6-F3, 7-D12, 12-A1, 12-D7, 12-E8, 12-F5, 12-G1, 12-G3). 7

PREPARATION



(II)

The oxidation is carried out with oxidizing agent pref. N-chlorosuccinimide at ca. 1-4 (pref. ca. 1-2) mol. on (II) in a solvent at 0-50 (pref. 20-30)° C for 0.5-10 (pref. 1-3) hrs. ($R^{4'}$=H,alkyl).

EXAMPLE

1,3-Dimethyl-6-(4-ethylthiosemicarbazido)uracil (40 g) is